

### **Remarks**

Reconsideration of the application is respectfully requested in view of the foregoing amendments and following remarks. Claims 1-30 are pending. Claims 1-30 are rejected. Claims 1, 8, 11-13, 18 and 26 are amended herein.

### ***Interview Summary***

Applicant thanks the Examiner for his time during a telephonic interview on June 5, 2007, with Examiner Eric West present. Features of claim 1 and U.S. Pat. No. 6,503,720 to Wittwer et al. (Wittwer) were discussed.

In light of proposed language, the Examiner cited to Wittwer at col. 10, line 65, to col. 11, line 12 as possibly forming a rejection for the claim. After reviewing the cited section of Wittwer, Applicant finds sufficient language in the claim to distinguish over Wittwer.

In the above-indicated section, Wittwer does describe calculating "maximae of first derivatives, second derivatives and the minimae of second derivatives." In addition, Wittwer describes "plots [demonstrating] the linear relation between the calculated cycle number and the log 10 of analyte concentration, proving that...extrema...may be used for determining initial analyte concentrations." As understood by Applicant, the passage does not describe "finding where on a usable portion of a standard sigmoid curve the observation lies" because the plots (e.g., FIGS. 3A-3J) are of cycle number versus extrema of derivatives, not observations. Wittwer does not describe that an observation can be located on the plots nor does Wittwer describe how it could be.

Finally, the Examiner also pointed out that due to a guideline update, the rejections under 35 U.S.C. § 101 could be withdrawn if the invention is described in the Specification as having a practical application.

### ***Rejections under 35 U.S.C. § 101***

The Action rejects claims 1-11 and 13-29 under 35 U.S.C. § 101 as directed to non-statutory subject matter. In particular, the Examiner states in the Office action at page 2 that "[a]lthough the claims appear useful and concrete, there does not appear to be a tangible result claimed." Applicant respectfully traverses this rejection.

Computer programs are statutory when stored on a computer-readable medium.

A claimed computer-readable medium encoded with a computer program is a computer element which defines structural and functional interrelationships between the computer program and the rest of the computer which permit the computer program's functionality to be realized, and is thus statutory." MPEP 2106.01.I.

As claim 1 recites "One or more computer-readable media comprising computer-executable instructions..." and as a "computer-readable medium encoded with a computer program... is thus statutory," claim 1 should not be subject to a 35 U.S.C. § 101 rejection.

In addition, claim 1 is addressed to a method wherein "the concentration of a substance" is calculated. One of skill in the art would recognize that calculating the concentration of a substance has a practical application. For example, calculating the concentration of an antibody or other substance can be useful, practical application. (See, e.g., Application at pages 6-7). For at least these reasons, claim 1 and its dependent claims, 2-7, are allowable.

As claims 8 and 11 also recite "One or more computer-readable media comprising computer-executable instructions" and as a "computer-readable medium encoded with a computer program... is thus statutory," claims 8 and 11 should not be subject to a 35 U.S.C. § 101 rejection. In addition, claims 8 and 11 recite a method wherein "the concentration of a substance" is calculated. Therefore, the claimed invention has a practical application. For at least these reasons, claims 8 and 11 and dependent claims 9-10 are allowable.

Amended claims 13 and 18 recite "A computer-implemented method," wherein "the concentration of a substance" is calculated. Therefore, the claimed invention has a practical application. For at least these reasons, claims 13 and 18 and dependent claims 14-17 and 19-25 are allowable.

Claim 26 recites "A software system encoded on one or more computer-readable media." Because a "computer-readable medium encoded with a computer program... is thus statutory," claim 26 should not be subject to a 35 U.S.C. § 101 rejection. In addition, claim 26 recites a method wherein "the concentration of a substance" is calculated. Therefore, the claimed invention has a practical application. For at least these reasons, claim 26 and dependent claims 27-29 are allowable.

***Rejections under 35 U.S.C. § 102(a)***

The Action rejects claims 1-6, 8-11, 13-22 and 24-30 under 35 U.S.C. § 102(a) as being anticipated by U.S. Pat. No. 6,503,720 to Wittwer et al. (Wittwer). Applicant respectfully traverses this rejection.

Amended claim 1 is directed to one or more computer-readable media comprising computer-executable instructions for performing a method to calculate concentration of a substance in a test sample, the method comprising:

for at least one observation of a metric for the test sample, finding where on a usable portion of a standard sigmoid curve the observation lies, wherein the usable portion of the standard sigmoid curve is determined via a second derivative of the standard sigmoid curve, and the usable portion of the standard sigmoid curve comprises a range of a plurality of points; and

based on a location of the observation on the standard sigmoid curve, calculating a concentration of the substance.

For example, the Application describes “a usable portion” at page 3, lines 26-27, as “[f]or example, a range of points between two endpoints” and at page 4, lines 12-13, as “the portion of the sigmoid curve between the two bounds (e.g., endpoints).” Additionally, a usable portion is designated to be a range of a plurality of points along a curve in the Application at Figure 7. Claim 1 stands rejected over Wittwer. However, Wittwer does not teach or suggest each and every element of the claim.

Wittwer’s description of methods for quantifying the concentration of a nucleic acid in a nucleic acid sample does not anticipate at least “finding where on a usable portion of a standard sigmoid curve the observation lies, wherein the usable portion of the standard sigmoid curve is determined via a second derivative of the standard sigmoid curve, and the usable portion of the standard sigmoid curve comprises a range of a plurality of points.” Wittwer states at column 4, lines 16-29:

[A] method for quantifying an analyte is described . . . The method comprises the steps of contacting the analyte with an amplifying agent . . . The amount of amplification product will then be determined as a function of reaction time, and the first, second or nth order derivative of said function will be calculated . . . The maximum, zero value or minimum of said derivative will then be determined and the initial concentration of the analyte will be calculated from said maximum, zero value or minimum. (Emphasis added)

Thus, Wittwer does describe determining a second derivative of a function. However, Wittwer does not “[find] where on a usable portion of a standard sigmoid curve the observation lies...[wherein] the usable portion of the standard sigmoid curve comprises a range of a plurality of points.”

For at least these reasons, claim 1 and its dependent claims 2-6 are allowable over Wittwer.

Amended claim 8 is directed to one or more computer-readable media comprising computer-executable instructions for performing a method to calculate concentration of a substance in a test sample, the method comprising:

for a plurality of observations of a metric for the test sample, fitting a test sigmoid curve to the observations; and

calculating a concentration of the substance in the test sample via the test sigmoid curve and a usable portion of a standard curve, wherein the usable portion of the standard sigmoid curve is determined via a second derivative of the standard sigmoid curve, and the usable portion of the standard curve comprises a range of a plurality of points.

Claim 8 stands rejected over Wittwer. However, Wittwer does not teach or suggest each and every element of the claim.

Wittwer's description of methods for quantifying the concentration of a nucleic acid in a nucleic acid sample does not anticipate at least “calculating a concentration of the substance in the test sample via the test sigmoid curve and a usable portion of a standard curve, wherein the usable portion of the standard sigmoid curve is determined via a second derivative of the standard sigmoid curve, and the usable portion of the standard sigmoid curve comprises a range of a plurality of points.” Wittwer states at column 12, lines 14-15 and lines 22-23:

The second derivative maximum is calculated to give a fractional cycle number of the control sample (T)...The potency of inhibition can be quantified by the magnitude and direction of the shift in fractional cycle number

Thus, Wittwer does describe determining a second derivative and determining a fractional cycle number. However, Wittwer does not “[calculate] a concentration of the substance in the test sample via the test sigmoid curve and a usable portion of a standard curve...[wherein] the usable portion of the standard sigmoid curve comprises a range of a plurality of points.”

For at least these reasons, claim 8 and its dependent claims 9-10 are allowable over Wittwer.

Amended claim 11 is directed to one or more computer-readable media comprising computer-executable instructions for performing a method to calculate concentration of a substance in a test sample, the method comprising:

- finding a usable portion of a sigmoid curve, wherein the usable portion of the sigmoid curve is determined via a second derivative of the sigmoid curve, and the usable portion of the sigmoid curve comprises a range of a plurality of points; and
- calculating a concentration of the substance in the test sample via the usable portion of the sigmoid curve.

Claim 11 stands rejected over Wittwer. However, Wittwer does not teach or suggest each and every element of the claim.

Wittwer's description of methods for quantifying the concentration of a nucleic acid in a nucleic acid sample does not anticipate at least "finding a usable portion of a sigmoid curve, wherein the usable portion of the sigmoid curve is determined via a second derivative of the sigmoid curve, and the usable portion of the sigmoid curve comprises a range of a plurality of points." Wittwer states at column 5, lines 3-8:

- c) calculating the first, second, or nth derivative of said function, wherein n is a natural number,
- d) determining the maximum, zero value, or minimum of said derivative, and
- e) calculating from said maximum, zero value, or minimum the initial concentration of the analyte.

Thus, Wittwer does describe calculating a derivative of a function. However, Wittwer does not "[find] a usable portion of a sigmoid curve,...[wherein] the usable portion of the sigmoid curve comprises a range of a plurality of points."

For at least these reasons, claim 11 is allowable over Wittwer.

Amended claim 13 is directed to a computer-implemented method of calculating concentration of a substance in a test sample having an unknown concentration of the substance, the method comprising:

- determining a usable portion of a sigmoid curve fit to data points representing observations of a reference sample having a known concentration of

the substance, wherein the usable portion of the sigmoid curve comprises a range of a plurality of points; and

calculating the concentration of the substance in the test sample based on a subset of observations of the test sample, wherein the subset is associated with the usable portion of the sigmoid curve.

Claim 13 stands rejected over Wittwer. However, Wittwer does not teach or suggest each and every element of the claim.

Wittwer's description of methods for quantifying the concentration of nucleic acid in a nucleic acid sample does not anticipate at least "determining a usable portion of a sigmoid curve fit to data points representing observations of a reference sample having a known concentration of the substance, wherein the usable portion of the sigmoid curve comprises a range of a plurality of points; and calculating the concentration of the substance in the test sample based on a subset of observations of the test sample, wherein the subset is associated with the usable portion of the sigmoid curve." Wittwer states at column 5, lines 3-8:

- c) calculating the first, second, or nth derivative of said function, wherein n is a natural number,
- d) determining the maximum, zero value, or minimum of said derivative, and
- e) calculating from said maximum, zero value, or minimum the initial concentration of the analyte.

Thus, Wittwer does describe calculating a concentration. However, Wittwer does not calculate the concentration based on "observations . . . associated with the usable portion of the sigmoid curve." Wittwer does not determine "a usable portion of a sigmoid curve" when calculating the concentration, nor does Wittwer describe a range of a plurality of points of a curve.

For at least these reasons, claim 13 and its dependent claims 14-17 are allowable over Wittwer.

Claim 18 is directed to a computer-implemented method of determining the concentration of antibody in a blood serum sample, the method comprising:

receiving a measurement of concentration of live cells in a test sample, wherein the test sample is generated by adding the serum to cells and a toxin neutralized by the antibody;

determining whether the concentration of live cells falls within a usable portion of a standard sigmoid curve representing observations taken of a sample having a known concentration of antibody, wherein the usable portion of the standard sigmoid curve comprises a range of a plurality of points; and

responsive to determining the concentration of live cells falls within the usable portion, calculating a concentration via the standard sigmoid curve.

Claim 18 stands rejected over Wittwer. However, Wittwer does not teach or suggest each and every element of the claim.

Wittwer's description of methods for quantifying the concentration of nucleic acid in a nucleic acid sample does not anticipate at least "determining whether the concentration of live cells falls within a usable portion of a standard sigmoid curve..., wherein the usable portion of the standard sigmoid curve comprises a range of a plurality of points; and responsive to determining the concentration of live cells falls within the usable portion, calculating a concentration via the standard sigmoid curve." Wittwer states at column 4, lines 26-29:

The maximum, zero value or minimum of said derivative will then be determined and the initial concentration of the analyte will be calculated from said maximum, zero value or minimum

Thus, Wittwer does describe calculating a concentration. However, Wittwer does not determine whether the concentration "falls within a usable portion of a standard sigmoid curve" and Wittwer does not calculate the concentration responsive to the determination. Further, Wittwer does not determine a "usable portion of the standard sigmoid curve" nor does Wittwer determine a range of a plurality of points of a curve.

For at least these reasons, claim 18 and its dependent claims 19-25 are allowable over Wittwer.

Amended claim 26 is directed to a software system encoded on one or more computer-readable media, the software system comprising:

- a representation of a characteristic sigmoid curve;
- means for designating a usable portion of the characteristic sigmoid curve, wherein the usable portion of the characteristic sigmoid curve comprises a range of a plurality of points;
- means for receiving at least one observation of a test sample;
- means for determining whether the observation of the test sample is within the usable portion of the characteristic sigmoid curve; and
- means for calculating a concentration for the observation responsive to determining that the observation is within the usable portion of the characteristic sigmoid curve.

Claim 26 stands rejected over Wittwer. However, Wittwer does not teach or suggest each and every element of the claim.

Wittwer's description of methods for quantifying the concentration of nucleic acid in a nucleic acid sample does not anticipate at least "means for designating a usable portion of the characteristic sigmoid curve, wherein a usable portion of the characteristic sigmoid curve comprises a range of a plurality of points...and means for calculating a concentration for the observation responsive to determining that the observation is within the usable portion of the characteristic sigmoid curve." Wittwer states at column 4, lines 16-29:

[A] method for quantifying an analyte is described . . . The method comprises the steps of contacting the analyte with an amplifying agent . . . The amount of amplification product will then be determined as a function of reaction time, and the first, second or nth order derivative of said function will be calculated . . . The maximum, zero value or minimum of said derivative will then be determined and the initial concentration of the analyte will be calculated from said maximum, zero value or minimum.

Thus, Wittwer does describe calculating a concentration. However, Wittwer does not describe designating a range of a plurality of points of a curve. Further, Wittwer does not describe calculating the concentration responsive to "determining that the observation is within the usable portion of the characteristic sigmoid curve."

For at least these reasons, claim 26 and its dependent claims 27-29 are allowable over Wittwer.

Claim 30 is directed to one or more computer-readable media comprising computer-executable instructions for performing a method to indicate presence of a substance in a test sample, the method comprising:

for at least one observation of a metric for the test sample, determining whether the observation is higher than a threshold value, wherein the threshold value is determined via a first derivative of a standard sigmoid curve; and responsive to determining the observation is higher than the threshold value, indicating presence of the substance.

Claim 30 stands rejected over Wittwer. However, Wittwer does not teach each and every element of the claim.

Wittwer's description of methods for quantifying the concentration of nucleic acid in a nucleic acid sample does not anticipate at least "for at least one observation of a metric for the



test sample, determining whether the observation is higher than a threshold value, wherein the threshold value is determined via a first derivative of a standard sigmoid curve; and responsive to determining the observation is higher than the threshold value, indicating presence of the substance.” The Action relies on the following description in Wittwer column 8, lines 40-57:

According to the previously disclosed method, *a manually chosen threshold level* was set after appropriate background subtraction of raw fluorescent data. For each sample, the intersection between the threshold line and the function of fluorescent signal versus time was calculated with the following algorithm: Based on a regression calculation, two measured points above a previously defined noise band were used to define a log linear phase by means of linear regression. Within the log linear area, a threshold line was set manually, and the intersection between the threshold line and the regression lines corresponding to each tested copy number were calculated. In order to gain information on the validity of the method, the calculated crossing points were used to create a plot indicating cycle number versus calculated log 10 of initial concentrations of the target DNA (see FIGS. 1A and 1B). (emphasis added)

Thus, Wittwer does describe a threshold. However, Wittwer does not describe a threshold value “that is determined via a first derivative of a standard sigmoid curve.” Further, Wittwer does not describe “indicating presence of the substance” responsive to “determining the observation is higher than the threshold value.”

For at least these reasons, claim 30 is allowable over Wittwer.

#### ***Rejections under 35 U.S.C. § 103(a)***

The Action rejects claims 7, 12 and 23 under 35 U.S.C. § 103(a) over Wittwer in view of U.S. Pat. Publication No. 2002/0160012 to Kaastrup (Kaastrup). Applicant respectfully traverses this rejection.

Claim 7 depends from claim 1 and is directed to one or more computer-readable media comprising computer-executable instructions for performing a method to calculate concentration of a substance in a test sample, the method comprising:

for at least one observation of a metric for the test sample, finding where on a usable portion of a standard sigmoid curve the observation lies, wherein the usable portion of the standard sigmoid curve is determined via a second derivative of the standard sigmoid curve, and the usable portion of the standard sigmoid curve comprises a range of a plurality of points; and

based on a location of the observation on the standard sigmoid curve, calculating a concentration of the substance in the test sample,

wherein the observation indicates optical density for the test sample,  
wherein the concentration indicates an amount of antibody in the test  
sample, and  
wherein the concentration indicates an amount of anti-PA IgG in the test  
sample.

Claim 7 stands rejected over Wittwer in view of Kaastrup. However, neither Wittwer alone nor Wittwer in combination with Kaastrup teaches each and every element of the claim.

Applicant has already stated reasons for the allowance of claim 1 (from which claim 7 depends) over Wittwer. Kaastrup is directed to a vaccine chip technology that exploits the immunostimulating effects of a fragment of TGF $\beta$  for immunization and other medical treatments. Kaastrup is silent on calculating derivatives and on determining "a usable portion" of a curve. Kaastrup does not cure the deficiencies of Wittwer.

For at least these reasons, claim 7 is allowable over Wittwer alone or in view of Kaastrup.

Claim 12 is directed to one or more computer-readable media comprising computer-executable instructions for performing a method comprising:

for a plurality of dilutions of a test sample, receiving respective measurements of optical density indicating concentration of live cells within the dilutions;

via the measurements, calculating a concentration of anti-PA IgG for the test sample via a usable portion of a sigmoid curve representing concentrations of live cells within dilutions of a reference sample having a known quantity of anti-PA IgG, wherein the sigmoid curve is represented via a four-parameter logistic technique, and wherein a usable portion of the sigmoid curve is determined via a second derivative of the sigmoid curve, and wherein the usable portion of the sigmoid curve comprises a range of a plurality of points; and  
indicating the concentration of anti-PA IgG for the test sample.

Claim 12 stands rejected over Wittwer in view of Kaastrup. However, neither Wittwer alone nor Wittwer in combination with Kaastrup teaches each and every element of the claim.

Claim 12 recites "a plurality of points," which is absent from Wittwer. Kaastrup is directed to a vaccine chip technology that exploits the immunostimulating effects of a fragment of TGF $\beta$  for immunization and other medical treatments. Kaastrup does not cure the deficiencies of Wittwer.

For at least these reasons, claim 12 is allowable over Wittwer alone or in view of Kaastrup.

Claim 23 depends from claim 18 and is directed to a computer-implemented method, encoded on a computer-readable medium, of determining the concentration of antibody in a blood serum sample, the method comprising:

receiving a measurement of concentration of live cells in a test sample, wherein the test sample is generated by adding the serum to cells and a toxin neutralized by the antibody;

determining whether the concentration of live cells falls within a usable portion of a standard sigmoid curve representing observations taken of a sample having a known concentration of antibody, wherein the usable portion of the standard sigmoid curve comprises a range of a plurality of points; and

responsive to determining the concentration of live cells falls within the usable portion, calculating a concentration via the standard sigmoid curve, wherein the antibody is anti-PA IgG.

Claim 23 stands rejected over Wittwer in view of Kaastrup. However, neither Wittwer alone nor Wittwer in combination with Kaastrup teaches each and every element of the claim.

Applicant has already stated reasons for the allowance of claim 18 (from which claim 23 depends) over Wittwer. Kaastrup is directed to a vaccine chip technology that exploits the immunostimulating effects of a fragment of TGF $\beta$  for immunization and other medical treatments. Kaastrup does not cure the deficiencies of Wittwer.

For at least these reasons, claim 23 is allowable over Wittwer alone or in view of Kaastrup.

#### ***Request for Interview***

If any issues remain, the Examiner is formally requested to contact the undersigned attorney prior to issuance of the next Office Action in order to arrange a telephonic interview. It is believed that a brief discussion of the merits of the present application may expedite prosecution. Applicant submits the foregoing formal Amendment so that the Examiner may fully evaluate Applicant's position, thereby enabling the interview to be more focused.

This request is being submitted under MPEP § 713.01, which indicates that an interview may be arranged in advance by written request.

**Conclusion**

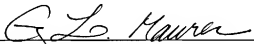
The claims in their present form should now be allowable. Such action is respectfully requested.

Respectfully submitted,

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